

Testing three theories of cognitive dysfunction in alcohol abuse

Analisi dei deficit neuropsicologici alcol-correlati alla luce di tre differenti ipotesi teoriche

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Summary

Objectives

Many hypotheses concerning the cognitive functions affected by chronic alcoholism have been advanced. The aim of this study was to test cognitive performance in a sample of alcoholics and to examine results comparing three different models: the frontal lobe hypothesis, the lateralisation hypothesis and the diffuse brain hypothesis.

Methods

Fifty-one patients who referred to an alcoholism service were included in this study. Cognitive functions were assessed by a trained psychologist using a specific neuropsychological battery.

Results

Our results show a ranking of degrees of impairment in different cognitive functions with dissimilar influence on clinical

features. In our sample, the frontal lobe hypothesis was disconfirmed. The results on right hemisphere seem to require more investigation and the generalized deficit hypothesis was not confirmed.

Conclusion

Cognitive deficits may compromise patients' utilisation of rehabilitative information. Increasing attention is being given to the opportunity to integrate specific support for cognitive functions in alcohol detox programmes. The first step in programming clinical intervention is to have a complete overview of the cognitive deficits in alcoholics.

Key words

Alcoholism • Cognition • Impairment • Theories • Cerebral lobes • Clinical features

Introduction

Alcohol abuse is a maladaptive pattern of drinking, leading to clinically-significant impairment or distress, as manifested by at least one of the following occurring within a 12-month period:

- recurrent use of alcohol resulting in a failure to fulfil major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to alcohol use; alcohol-related absences, suspensions, or expulsions from school; neglect of children or household);
- recurrent alcohol use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by alcohol use);
- recurrent alcohol-related legal problems (e.g., arrests for alcohol-related disorderly conduct);
- continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol (e.g., arguments with spouse about consequences of intoxication) ¹.

Research on alcoholism has two important aims: to evaluate existing therapies and to increase knowledge about the biology of alcoholism. Heavy alcohol intake is associated with both structural and functional changes in the central nervous system, with long-term neuronal adaptive changes contributing to the phenomena of tolerance and withdrawal symptoms ². Considerable progress has been made in the last 20 years regarding the physical mechanisms of addiction, theories of alcohol action in the human body and psychosocial effects of alcohol abuse ³. Despite these facts, it is still difficult to have a general view of the above knowledge since alcohol dependence is a heterogeneous disorder with many contributing factors that vary from person to person ⁴. Several studies have shown important variations in the presence and severity of different cognitive deficits. In fact, there is a gap between patients who do not present any kind of disorder and those who develop dementia ⁵.

The exact nature of the neuropsychological disorders related to alcoholism is still under discussion. New neuro-

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science techniques have led to an increased understanding of alcohol addiction and have permitted studies of the effects of alcohol on the brain. Both animal and human genetics studies are increasingly enabling the identification of genes that confer vulnerability to alcoholism. Issues requiring a great deal of further study include individual drinking patterns, the role of cognition in alcohol-seeking behaviour and the subjective effects of drinking⁶. The causes of cognitive impairment found in alcoholics include direct effects of alcohol toxicity, pre-existing cognitive deficits that predispose towards substance abuse, comorbid psychiatric disorders and abuse of substances other than alcohol⁷.

Studies on neuropsychological functions in alcoholism have reported different deficits including visual-spatial abilities, attention, memory, executive function and social cognition⁸. In particular, visual-spatial and explicit memory for visual-spatial stimuli deficits has been observed⁹. Greater deficits in executive functions compared with other cognitive functions have been reported, especially in problem solving, abstraction, planning, organising and working memory¹⁰. Working memory has been investigated in several studies and impairments have been often found¹¹. For Hildebrandt, the neurotoxic side effects of alcohol therefore lead to a specific deficit in alternating between response rules but not in working memory, independently of whether the working memory task involves interferences resolution or not¹². A study conducted in a Spanish sample showed poorer performance in tests related to attention control, performance speed, automatic response inhibition, visual-spatial function and visual memory¹³. A representative sample of alcoholics showed specific attention deficits as opposed to a general decline of attention at treatment intake. Thus, sober alcoholics appear to be as efficient as controls at selecting on the basis of location. Nonetheless, when they are required to respond to two independent sources of information, such as the divided attention task, they show impaired performance¹⁴. Previous studies are discordant on cognitive impairment in alcoholism: for example, in younger samples, cognitive impairment is more infrequent¹⁵. One of the most important goals of the evaluation is the recovery of cognitive deficits related to alcohol abuse; several cognitive deficits (perceptual motor speed, verbal short-term memory, verbal knowledge, non-verbal reasoning and spatial imagination) show significant improvement after 5 weeks of treatment¹⁶. Similar results have been found in an Australian sample: at baseline, chronic and episodic alcohol users showed impaired visual motor, learning, memory and executive function. Visual motor deficits had normalised within 11 months and other deficits had improved to normal levels within 4 weeks¹⁷. Throughout many studies educational attainment is only sometimes controlled, and is thus problematic. Krahn hypothesised

that the observed relationship between alcohol intake and cognition may change when this variable is controlled¹⁸. Moreover, alcoholics achieve significantly lower scores than controls on summery indices of the Wechsler Memory and Adult Intelligence Scales and showed greater decline from estimated premorbid intelligence levels than controls¹⁹. High level cognitive processes are also an important field of research. Some theories of mind and deficit in executive functions have been found and could be of relevance in investigating their impact on rehabilitation programmes²⁰.

The exact nature of the neuropsychological disorders related to alcoholism is still under discussion and the most recent investigations have proposed different hypotheses. The first hypothesis is known as "frontal lobe" hypothesis and states that the frontal lobes are most vulnerable to the effects of alcohol. There is agreement upon the specificity of cognitive functions related to the frontal lobe, called "executive functions"²¹. More precisely, these functions include: cognitive flexibility, speed in allocation of attentional resources, shifting ability, speed in information processing, inhibition of perseverative errors, perceptual motor speed, abstractive and planning abilities and suppression of irrelevant information. Findings in alcoholics suggesting deficits on abstracting and problem solving tests, support this hypothesis. Difficulties in categorising and inflexibility of thinking, as measured by different instruments, could be related to selective frontal lobe dysfunction, even in the absence of severe global impairment²²⁻²³.

In support of the frontal lobe hypothesis, findings from multiple neuropsychological studies have revealed diminished functioning in problem solving, abstraction, working memory, attention and response inhibition/impulsivity²⁴⁻²⁹. Different studies have demonstrated a loss of neurons, primarily from the frontal cortex³⁰⁻³⁴. These studies suggest that the frontal lobes are more susceptible to ethanol damage than other brain regions. However, other studies have either found a lack of dysfunction in the frontal lobes or have revealed deficits in other regions, negating the hypothesis of frontal lobe exclusivity³⁵⁻³⁷. These contrasting findings require further investigation.

The second hypothesis is the "lateralisation hypothesis", which states that right hemisphere functions are more susceptible to the neurotoxic effects of alcoholism³⁸. The right hemisphere has a role in selective attentional processing and has the ability to attend to the spatial array. The pattern of results in alcoholics is consistent with the right hemisphere model of alcoholism-related cognitive decline³⁹.

Comparison between verbal and non-verbal tasks has shown that impairment of visual learning, visual memory and visuospatial abilities are often be found and seem to be more resistant to recovery⁴⁰⁻⁴².

The “diffuse brain dysfunction” hypothesis considers that alcohol affects all areas of the brain. A review by Parsons⁴³ described findings from cross-sectional and longitudinal studies; these results revealed verbal, visuospatial and abstracting deficits that support the diffuse brain hypothesis. The cognitive deficits showed by sober alcoholics include impairment in different functions, such as verbal and non-verbal thinking, verbal and non-verbal learning, memory, visuospatial perception and perceptual motor skills^{44 45}. This pattern of deficits is consistent with the hypothesis that chronic alcoholism produces mild generalised brain dysfunction.

While studies frequently make allusion to each of these three hypotheses, inconsistent findings have been reported that do not always support the assumptions of one specific theory. The aim of this study was to test cognitive performance in a sample of alcoholics and to examine the results to compare these different models.

Methods

Participants

A total of 110 alcohol-dependent individuals were consecutively recruited from the alcohol-dependence service of San Raffaele Hospital in Milan, Italy at admission.

All subjects were given an assessment, which took approximately three hours and included an anamnestic interview and a neuropsychological battery that was administrated by trained technicians of the psychological service within the first week after admission, or as soon as the patient was clinically stable enough to undergo testing.

Patients who had previously been diagnosed with any disorder from DSM-IV TR Axis 1 (other than substance dependence) were not included. Moreover, patients with concurrent neurological diseases and traumatic brain injury were excluded as were those with a MODA score < 89 (30 patients were classified as insufficient).

The final sample included 51 subjects (33 men; 18 women), aged between 27 and 69 years old (47.00 ± 9.88) with school attendance that ranged from 6 to 18 years (12.67 ± 3.18). The concurrent use of substances other than alcohol was also evaluated: 37.2% of patients ($n = 19$) have reported no substance use, 54.9% of the sample ($n = 28$) referred substance use in the past and 7.9% ($n = 4$) were using substances at admission.

All participants were native Italian speakers and accepted the informed consent. No remuneration was given. The study protocol was approved by the hospital's ethics committee.

Procedures

Measures

The neuropsychological battery included Brief Assessment of Cognition in Schizophrenia (BACS) and Milan Overall Dementia Assessment (MODA). BACS includes the following subtests: verbal memory (word recall); working memory (digit sequencing); token motor task (psychomotor speed and coordination); selective attention (symbol coding); semantic fluency; letter fluency; Tower of London. Verbal memory tasks were adapted to Italian by substituting English words with Italian words that were matched for frequency and phonemic characteristics. The letter fluency tasks were adapted using letters that were already used in common Italian clinical tests for letter fluency. Verbal memory and Tower of London tasks consist of two alternative forms for repeated measures assessment⁴⁶. The BACS scores were analysed by simultaneous multiple regression to assess the influence of age, education and gender. For each score, a linear regression model was applied to adjust original score for age, education and gender. The cut-off score indicates the score below which the probability that an individual belongs to the normal population is less than 0.05, with a confidence level of 0.95. Norms were computed with the equivalent scores method⁴⁷ to enable comparison with other neuropsychological tasks commonly used in Italy⁴⁸⁻⁵⁰, such as Wisconsin card sorting test, Stroop colour-word tests and Raven's progressive matrices. Adjust scores were fitted into a 5-point interval scale to obtain equivalent score, that was classified as follows: limit for pathological performance = 0; borderline value = 1; intermediate value = 2 or 3; equal or better than median value = 4⁵¹.

MODA is a short, neuropsychological oriented test used for assessment of dementia. MODA is a paper and pencil test composed of three sections: a behavioural scale and two testing sections. The three sections are given in the same testing session in the same sequence. The behavioural component (autonomy scale) accounts for 15% of the score and comprises a set of items that assess everyday coping skills. Information is provided by a relative and can therefore be collected even in cases of severe deterioration. The cognitive contribution represents 85% of the total score (orientation enquiry and neuropsychological testing yield, respectively, 35% and 50% of the overall score). The MODA total score ranges from the worst of 0 to the best of 100. In all items, a score of zero is given if the patient fails to provide an answer or responds inappropriately. Instructions may be repeated for each item, so as to elicit the patient's best possible performance⁵².

Results

Descriptive statistics

Table I shows the descriptive statistics of the subtest score considering the different grade of impairment in cognitive functions. Equivalent scores allow considering scores 0 and 1 as “deficient”. These results demonstrate the dissimilar grades of impairment between the different cognitive functions.

In each BACS subtest, correction grids were used to adjust the performance of each subject in term of education, age and sex. Single subtest scores are shown in Table I.

Considering equivalent score it is possible to state that, in our sample, the lowest-scoring functions are attention and speed of information processing, which had mean of 1.47 ± 1.50 . Motor speed and coordination had mean of 1.90 ± 1.50 ; these results appear to confirm the relationship between alcohol abuse and low functioning of the motor system. Verbal fluency showed a mean of 2.12 ± 1.27 . Verbal memory and working memory had higher results than other functions with means of 2.74 ± 1.41 and 2.47 ± 1.28 , respectively. The Tower of London task showed the highest results and the lowest dispersion with mean of 3.33 ± 1.11 .

Table II shows that age had a significant relationship with

TABLE I.
Descriptive statistics. *Statistiche descrittive.*

	Min.	Max.	Mean	S.D.	Median	Interquartile range	Percentages of deficient participants (e.s.0 + e.s.1)
Verbal Memory Correct Score	27.75	67.75	47.40	10.39	48.75	18.00	-
Verbal Memory E.S.	0.00	4.00	2.74	1.41	3.00	3.00	27.5%
Working Memory Correct Score	12.50	31.25	20.63	4.38	20.25	6.25	-
Working Memory E.S.	0.00	4.00	2.47	1.29	3.00	3.00	27.5%
Motor Speed Correct Score	44.00	100.00	76.94	14.83	77.75	22.00	-
Motor Speed E.S.	0.00	4.00	1.90	1.50	2.00	2.00	45.1%
Verbal Fluency Correct Score	26.25	68.50	44.47	9.72	45.25	14.75	-
Verbal Fluency E.S.	0.00	4.00	2.12	1.27	2.00	2.00	33.3%
Attention and speed of processing Correct Score	27.00	77.50	45.75	11.72	43.75	15.75	-
Attention and speed of processing E.S.	0.00	4.00	1.47	1.50	1.00	3.00	58.8%
Tower of London Correct Score	10.00	22.50	18.60	3.15	19.00	4.00	-
Tower of London E.S.	0.00	4.00	3.33	1.11	4.00	1.00	11.1%

Min.: minimum score; Max.: maximum score; S.D.: standard deviation; E.S.: equivalent score.

TABLE II.
Impact of clinical features. *Impatto delle caratteristiche cliniche.*

Function	Age	Education	Other substances abuse	Sex
Verbal Memory ES	n.s.	n.s.	n.s.	n.s.
Working Memory ES	n.s.	n.s.	n.s.	n.s.
Motor Speed ES	-0.366 (p < 0.01)	n.s.	n.s.	n.s.
Verbal Fluency ES	n.s.	n.s.	n.s.	n.s.
Attention and speed of information processing ES	n.s.	0.343 (p < 0.05)	n.s.	n.s.
Tower of London ES	n.s.	n.s.	n.s.	n.s.

E.S.: equivalent score; n.s.: non significant.

motor speed and coordination. Education had a direct relationship on attention and speed of information processing. Polyabuse condition did not show any impact on cognitive performance in comparison with only alcohol abuse alone. there was no association of gender with cognitive performance.

Correlations were used to assess the effect of age and education because it was not possible to assume population discontinuity in specific classes. Age had a significant relationship with motor speed and coordination, and the worst performances were found in older patients (correlation: -0.37). Education had a direct relationship on attention and speed of information processing (correlation: 0.34). The Mann-Whitney non-parametric test allows us explore the impact of dicotomic variables as polyabuse and sex on cognitive performance. As there were no significant differences, this suggests that polyabusers do not have worse cognitive performance in comparison with alcoholics alone. Gender had no relationship with cognitive functions.

Comparison of different cognitive functions

To evaluate the differences within the different cognitive function, in order to determine which hypothesis is the most reliable, we applied Friedman's ANOVA on the equivalent score totalised in the assessment session using the BACS battery. To evaluate the post-hoc test, we utilised the Wilcoxon test, adjusting the confident interval by Bonferonni's methodology ($\alpha = 0.05/5 = .01$).

Frontal Lobe Hypothesis: we have compared the Tower of London equivalent score with other cognitive performances to determine if the frontal functions were the most deteriorated, according to the hypothesis mentioned earlier. The Tower of London showed an equivalent score that was significantly higher than all other cognitive functions (Tab. III). Therefore, is possible to conclude that frontal functions are less impaired in alcohol dependent patients, refuting the frontal lobe hypothesis.

TABLE III.
Frontal lobe hypothesis. *Ipotesi dei lobi frontali.*

Tower of London E.S. vs.	Z	p
Verbal Memory E.S.	-3.12	p < 0.01
Working Memory E.S.	-3.87	p < 0.001
Motor Speed E.S.	-4.92	p < 0.001
Verbal Fluency E.S.	-4.34	p < 0.001
Attention and speed of information proc. E.S. sing. E.S.	-5.56	p < 0.001

E.S.: equivalent score. A negative Z score indicates that it is higher than the score with which it has compared.

TABLE IV.
Lateralisation hypothesis. *Ipotesi della lateralizzazione.*

	Z	p
Verbal Memory E.S. vs Verbal Fluency E.S.	-2.11	p > 0.01 (n.s.)
Verbal Memory E.S. vs Motor Speed E.S.	-2.98	p < 0.01
Verbal Memory E.S. vs Symbol Coding E.S.	-4.95	p < 0.001
Verbal Fluency E.S. vs Verbal Memory	-2.11	p > 0.01 (n.s.)
Verbal Fluency E.S. vs Motor Speed E.S.	-0.88	p > 0.05 (n.s.)
Verbal Fluency E.S. vs Symbol Coding E.S.	-2.82	p < 0.01

E.S.: equivalent score; n.s.: non significant. A negative Z score indicates that it is higher than the score with which it has compared.

Table III shows the that the Tower of London equivalent score was significantly higher than all the other cognitive functions Therefore, is possible to conclude that the frontal functions are less impaired in alcohol dependent patients, negating the frontal lobe hypothesis.

For the lateralisation hypothesis we compared the results of verbal and non-verbal tasks. Verbal tasks were measured by the subtests of Verbal Memory and Verbal Fluency, while the non-verbal tasks were represented by the Motor Speed and Symbol Coding subtests. The results only partially confirm the lateralisation hypothesis. Verbal memory showed significantly higher results than non-verbal tasks. Verbal fluency had no significant association with motor speed (Tab. IV).

Table IV shows that verbal memory had significantly higher results than non-verbal tasks. Verbal fluency had no significant differences with motor speed.

For the diffuse brain dysfunction hypothesis we have compared the results of all tasks in order to determine if all cognitive functions had the same level of impairment according to the above-described hypothesis (Tab. V). While it was possible to rank degree of impairment in different cognitive functions, the results are in contrast with the diffuse brain dysfunction hypothesis.

Table V shows that different cognitive functions are affected to various degrees by alcohol intake. It is not possible to confirm the diffuse brain dysfunction hypothesis.

Discussion

Cognitive impairment is a core feature of chronic alcoholism. Between 50% and 80% of individuals with alcohol use disorders experience mild to severe neu-

TABLE V.
Diffuse brain dysfunction hypothesis. *Ipotesi di deficit diffuso.*

	Z	p
Working Memory vs Verbal Memory ES	-1.31	n.s.
Working Memory vs Motor Speed ES	-2.69	p < 0.01
Working Memory vs Verbal Fluency ES	-1.92	n.s.
Working Memory vs Symbol Coding ES	-4.15	p < 0.001
Motor Speed ES vs Symbol Coding ES	-1.93	n.s.

E.S.: equivalent score; n.s.: non significant. A negative Z score indicates that it is higher than the score with which it has compared.

rocognitive impairment. Current treatments for alcohol abuse disorders focus on changing behaviour and developing skills to prevent relapse and promote psychosocial adaptation, activities that clearly require cognitive processing⁵³⁻⁵⁶. The relationship between cognitive impairment and alcoholism treatment is still under discussion. Clinical experience suggests that alcohol-related neuropsychological impairment affects treatment outcome, but research on addiction have provided few indications in this direction. Bates, Bowden and Barry have explored this aspect by testing five different models of the relationship between neuropsychological impairment and addiction treatment outcome⁵⁷. Their findings do not support a direct influence of cognitive impairment on outcome, but suggest that it could be a moderator variable which impacts the action and strength of risk factors.

The principal aim of this study was to investigate the theoretical framework explaining cognitive impairment related to alcohol abuse by testing different hypotheses in a clinical sample.

The descriptive analysis allowed us to compare single subtest scores and to use them to investigate different hypotheses. It was possible to conclude that the scores in executive functions task (Tower of London task) are significantly higher than the one in other functions; Verbal Memory is the second less impaired function, with significant differences in motor speed, attention and speed of information processing. The third most preserved function is Working Memory. In contrast, the most impaired functions include Attention and Speed of information processing, and show significantly lower scores than Tower of London, Verbal Memory and Working Memory tasks. Motor speed showed a significantly lower level than London Tower and Verbal Memory task, and Verbal Fluency had lower significantly

scores only compared to Tower of London, which showed significantly higher scores than other functions.

This result underlines that frontal functions are the most resilient to alcohol damage and do not confirm the frontal lobe hypothesis. These results thus require a further investigation. In order to test the lateralisation hypothesis, we compared verbal and visual-spatial functions. Verbal memory showed a higher score than both psychomotor speed and symbol coding tasks. These results would seem to confirm the lateralisation hypothesis, although verbal fluency had no significant differences with visual-spatial functions. Therefore, the lateralisation hypothesis cannot be completely confirmed.

Our results show significant differences between the BACS subtests. It is possible to rank different degrees of impairment in different cognitive functions, and the results are in contrast with the diffuse brain dysfunction hypothesis, which considers the same level of impairment between different functions. Speed of processing, verbal fluency, psychomotor speed and coordination seem to be most impaired functions; these abilities presume the presence of preserved executive speed. These results appear to be in agreement with the hypothesis that alcohol significantly slows total information processing.

The results of the present study must be considered in light of several limitations. The small size of our sample could influence the possibility of generalising our conclusions. The absence of a control group is due to the aim of this study: in fact, our principal purpose was to compare different hypotheses about the exact nature of neuropsychological disorders related to alcoholism. The small size of our sample makes it difficult to attribute the results to alcohol consumption; otherwise, the equivalent score method assumes that the corrections based on normative sample are applicable to small samples and, in addition the influence of principal clinical features (i.e. age, sex, scholarship and polyabuse) on cognitive performance must be taken into consideration.

The relationship between cerebral lobes and neuropsychological measures shows complex patterns; cerebral lobes are multifunctional structures and a single neuropsychological measure could seem inadequate to test their functioning. Nevertheless, our results are supported by findings in the literature. The Tower of London task is thought to depend on planning ability, a capacity requiring intact frontal-lobe functioning.

Comparing Korsakoff and non-Korsakoff alcoholics, Joyce and Robbins have demonstrated that only Korsakoff patients show impairment in this task. Moreover, the deficit in Korsakoff patients in this task is not due to impairment in visuospatial skills or memory, but to impairment in planning ability⁵⁸. Smith and Jonides, using a threshold-independent measure of hemispheric lateralisation, demonstrated that brain activity during verbal working memory showed a more left-hemisphere lateralised pattern of BOLD response, par-

ticularly in the frontal and parietal lobes, while spatial working memory invoked a pattern of more right-hemisphere lateralised activity, observed in both frontal and temporal lobe regions. This pattern is consistent with the literature in adults showing this hemispheric distinction⁵⁹.

Many authors have recently pointed out the necessity of considering intervenient phenomena during cognitive assessment. Cohen and Maunsell underline that it is impossible to control a subject's internal state completely, so that fluctuations in cognitive states, such as attention, must occur in all experiments⁶⁰. The experimental evidence suggests that mind-wandering may be one of the most ubiquitous and pervasive of all cognitive phenomena. Taking into account multiple tasks, verbal reports have indicated that participants seem to spend 15-50% of the time mind-wandering. The possible relationship between mind-wandering and our results will be considered in a future study.

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Conflict of interests

There is no conflict of interest.

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